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EXAMINER	
ARCHIE, NINA	
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1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,971	HAPPE ET AL	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-105* is/are pending in the application.

4a) Of the above claim(s) *1-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-39 and 41-105* is/are rejected.

7)☐ Claim(s) *40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/12/2004, 5/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

2. The information disclosure statement filed 7/12/2004 and 5/20/2005 have been considered. Initialed copies are enclosed.

Election/Restrictions

3. Applicant's election with traverse of Group III (claims 28-105) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Group 1 (claims 1-3), Group II (claims 4-27) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement on 1/3/2007.

It is noted that Applicants request rejoinder when the claims of Group I become allowable.

Examiner withdraws the elections of species and SEQ ID NOs. 1-5 has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 28-39 and 41-105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 28, 42, 58, 74, and 90 independent claims and all dependent claims 29-41, 43-57, 59-73, and 75-105 are drawn to a method of detecting the presence of a *Mycoplasma* species in a sample, the method comprising: forming a reaction mixture comprising the sample and a set of oligonucleotide primers that hybridize under standard conditions to a nucleic acid sequence comprised by a *Mycoplasma* 16S rRNA gene, wherein the 3'-terminal nucleotide of one or more of said set of primers is selected so as not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a *Mycoplasma* species in said sample (claim 28); a method for detecting the presence of a Mycoplasma species in a sample, the / method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO: 2;

extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample (claim 42); a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO. 1; extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample (claim 58); a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO. 3; extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample (claim 74); a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO. 4; extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample (claim 90).

The specification discloses specific primers that are used to detect eight different species of Mycoplasma. The specification discloses primer sequences that are conserved with particular Mycoplasma species (see specification pgs. 27-28). The specification and claims do not indicate what distinguishing attributes all members of the genus share. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members are permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, using primers to detect Mycoplasma species alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that

the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant's claims fail to disclose how a set of primers comprising SEQ ID NOs. 1-4 is generated. Detecting such sequences within a sample is routine in the art, however generating such primers in the first place requires knowledge of the specific primers and probes used to amplify the particular sequences. Without disclosure of the particular primers and probes are generated, Applicants written description requirement is not deemed to be fulfilled. Furthermore, Applicants have disclosed the precise primers represented by SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4 words in other words "consisting of" the identified primer. Applicant's disclosure fails to identify the upstream or downstream regions of this fragment, which will have a profound impact on the activity of the molecule. Accordingly, the written description of the primer is sufficient only for the identified fragment, i.e., "consisting of." However, the written description requirement for these primers is also only satisfied for the described primer, i.e., consisting of. Additional nucleotides on either side of the identified primer will dramatically alter its binding interaction with other DNA molecules. Therefore, the specification lacks written description of the claimed method of detecting the presence of a Mycoplasma species in a sample. This issue is best resolved by Applicants pointing to the specification by page and line number where description of the claimed invention is set forth.

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

5. Claims 28-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting the presence of a *Mycoplasma* species in a sample using specific primers (SEQ ID. Nos. 1-4) does not provide enablement for a method of detecting the presence of *Mycoplasma* species in sample comprising forming a reaction mixture comprising any sample and any set of oligonucleotide primers that hybridize under standard conditions to a nucleic acid

sequence comprised by a *Mycoplasma* 16S rRNA gene, wherein the 3'-terminal nucleotide of one or more of any set of primers is selected so as not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with an E. coli 16S rRNA gene template, extending any primers, and detecting extension products of any primers, wherein the presence of an extension product is indicative of the presence of all *Mycoplasma* species in any sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
(B)The nature of the invention;
(C)The state of the prior art;
(D)The level of one of ordinary skill;
(E)The level of predictability in the art;
(F)The amount of direction provided by the inventor;
(G)The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims. The product being used to detect all *Mycoplasma* species stated in claim 28, any set of oligonucleotide primers is overly broad. The structure of the set of oligonucleotide primers is not defined the primers only functional limitations.

The structure of the oligonucleotide primers is vast in view of the recitation of the open claim language of "comprising". The claims are drawn to a method for detecting the presence of all *Mycoplasma* species in any sample. Therefore it is hard for one skilled in the art to determine if any oligonucleotide primer can be used for detecting all *Mycoplasma* species. The quantity of experimentation required to practice the invention as claimed would require the determination of a universal set of oligonucleotide primers to detect all *Mycoplasma* species including novel and unknown species that will correlate to a universal oligonucleotide primer set with limitations as discussed above to detect the presence of all *Mycoplasma* species. Since the specification fails to provide particular guidance for detecting the presence of all *Mycoplasma* species in any sample with the limitation as set forth supra it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Nature of the invention. The claims are drawn to a method of detecting the presence of a *Mycoplasma* species in a sample, the method comprising: forming a reaction mixture comprising the sample and a set of oligonucleotide primers that hybridize under standard conditions to a nucleic acid sequence comprised by a *Mycoplasma* 16S rRNA gene, wherein the 3'-terminal nucleotide of one or more of said set of primers is selected so as not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a *Mycoplasma* species in said sample (claim 28); a method for detecting the presence of a *Mycoplasma* species in a sample, the / method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more *Mycoplasma* species, the set of oligonucleotide primers comprising SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4, extending at least one of said primers, and detecting an extension product, wherein the presence of an extension product indicates the presence of a *Mycoplasma* species in said sample (claims 42, 58, 74, and 90).

The specification discloses one set of oligonucleotide primers to detect eight different species of *Mycoplasma* (see Example 1 pg. 34). Example 2 discloses elimination of E. coli reactivity reduces false positives (see pgs. 36-37). Example 3 discloses the internal amplification control template used in reactions with and without *Mycoplasma* genomic DNA (see pgs. 37-38). Example 4 discloses assays of the eight species of *Mycoplasma* (see pgs. 38 and Table 3). Example 7 discloses the utility of the 16S primer set mtri1A/mtri1B/mtri1D/mtri2short, which are SEQ ID NOs. 1-4 for detecting *Mycoplasma* in a sample (see pgs. 41-42).

The state of the prior art. The state of the art is unpredictable with regard to detecting M*ycoplasma* using a set of oligonucleotide primers. The art shows that "from E. coli that all three rRNAs in the prokaryotic ribosome are synthesized in stoichiometric amounts". The art shows that the number of rRNA genes in different Mollicutes (i.e. Mycoplasma) species in general tends to be low (see Taschke et al 1986 Mol. Gen. Genet Vol. 205 pgs. 428-433). The art shows detection system that utilizes a denaturing gradient gel electrophoresis of a 16S ribosomal RNA PCR product was used to differentiate 32 Mycoplasma species. The art show the detection of all major M*ycoplasmas* of veterinary significance within a single test using universal bacterial primers. However the study suggest that the detection system could be used for *Mycoplasma* that are difficult to culture however the disadvantage is that bacteria other than *Mycoplasma* could also generate a band on the gel which may give confusing results and that specific Mycoplasma specific primers may overcome the problem (see McAuliffe et al Journal of Clinical Microbiology 2003 Vol. 41 No. 10 pgs. 4844-4847 in its entirety). The art indicates that further research should concentrate on optimizing the sample preparation procedure so that a large number of samples can be processed more rapidly without DNA carryover and less false positives (see van Kuppeveld et al 1994 Applied and Environmental Microbiology pgs. 149-152 especially pg. 152 column 2). The art shows that DNA probes were designed to aid in diagnoses of farm and laboratory and laboratory animals, and the hard to diagnose M*ycoplasma* infections of cell cultures. The art shows the sensitivity of M*ycoplasma* detection by the different probes ranged

between 10^3 and 10^6 colony forming units, a level which may not be sufficiently high for use in a clinical laboratory. The art shows that false positives results may occur due to contamination of the reagents with target DNA. The art shows a disadvantage of universal primers, which are defined in the art as primers with a wide specificity, which will react with the DNA of any *Mycoplasma* or even with the DNA of other prokaryotes. The art shows that "universal primers may be satisfactory for detection of *Mycoplasma* infection in cell cultures, where the goal is just to screen the cultures for contamination". The art shows "disadvantage to the use of universal primers, which are 1) some Gram positive bacteria that is phylogenetically related Mycoplasma and 2) universal primers cannot be used for diagnosis of *Mycoplasma* like organisms in plant material (3) contamination of any of the PCR reagents with bacteria, may lead to false positives". Further the art shows that "diagnostic tests based on DNA probes have not gained so far the status of routine tests, as their use is still technically demanding, and often they lack the sensitivity required" (see Razin et al 1994 Academic Press Vol. 6 pgs. 497-511 especially pg. 497, pg. 500 column 2, pg. 501 and pg. 511). Therefore, the state of the art shows that there are limitations species-specific primers to confirm the presence of Mollicutes in specimens and for identification and that the limited number of species-specific primers that have been described need to be evaluated for sensitivity and specificity to produce other primers before any primer to detect all Mycoplasma species can be widely accepted for routine use. For the reasons set forth supra, the state of the art is unpredictable with regard to detecting the presence of Mycoplasma using a set of oligonucleotide primers.

Guidance in the specification. The specification refers particular primers for the method of detecting Mycoplasma. The application contemplates that the detection of eight different Mycoplasma species using the set of oligonucleotide primers are sufficient to all Mycoplasma. Therefore, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful method for detecting all Mycoplasma using the oligonucleotide primers discussed above and known unpredictability associated with the ability to detect all

Mycoplasma species. Eventhough the specification give an example of a method for detecting eight different Mycoplasma species and address factors such as elimination of false positives. It is well know in the art that false positives result from the sensitivity of the polymerase chain reaction and DNA contamination to and cleanliness of lab station and adherence to a strict set of protocols can lessen and maybe prevent false positives. Therefore, the specification as filed fails to provide particular guidance demonstrating a reasonable extrapolation which resolves the known unpredictability in the art associated with detecting all Mycoplasma species using any set of oligonucleotide primer.

Working examples. The specification provides sufficient working examples of a particular set of oligonucleotide primers as set forth supra.

In conclusion, the claimed inventions are not enabled for a method of detecting the presence of Mycoplasma species in sample comprising forming a reaction mixture comprising any sample and any set of oligonucleotide primers that hybridize under standard conditions to a nucleic acid sequence comprised by a Mycoplasma 16S rRNA gene, wherein the 3'-terminal nucleotide of one or more of any set of primers is selected so as not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with an E. coli 16S rRNA gene template, extending any primers, and detecting extension products of any primers, wherein the presence of an extension product is indicative of the presence of all Mycoplasma species in any sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention. The product being used as a set of oligonucleotide primers stated in claims 28, 42, 58, 74, and 90 is overly broad. The specification gives a description of a particular set of oligonucleotide primers that detect Mycoplasma. The specification does not provide any evidence that at least one set of oligonucleotide primers can be used to detect all Mycoplasma species. The state of the art shows a set of oligonucleotides primers used to detect and differentiate *Mycoplasma* and that there are sets of oligonucleotide primers that could be useful in detecting major *Mycoplasma*

but not all *Mycoplasma* species and it is apparent from the state of the art that there are limitations as set forth supra unpredictable. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 28-32, 34-38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mckenzie et al. 1996 US Patent No. 5,491,062 Feb. 13, 1996 in view of Webster, D WO 03/006653A1 Filing date July 11, 2001, Hartley, J US Patent No. 5,035,996 July 30, 1991 and Dodge et al US Patent No. 6,054278 April 25, 2000.

Claims 28-32, 34-38 and 41 are drawn to a method of detecting the presence of a Mycoplasma species in a sample, the method comprising: forming a reaction mixture comprising the sample and a set of oligonucleotide primers that hybridize under standard conditions to a nucleic acid sequence comprised by a Mycoplasma 16S rRNA gene, wherein the 3'-terminal nucleotide of one or more of said set of primers is selected so as not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample.

Mckenzie et al teach a method of detecting the presence of a Mycoplasma species in a sample, the method comprising: forming a reaction mixture comprising the sample and a set of oligonucleotide primers that hybridize under standard conditions, wherein the step of extending said primers comprises polymerase chain reaction (PCR) amplification, wherein the reaction mixture further comprises an internal amplification control template, wherein the product of amplification of the internal amplification control template is detectably different in size or sequence than the product of amplification of M*ycoplasma* 16S rRNA species amplified in said sample, wherein a internal amplification control comprises a nucleic acid template comprising 5' and 3' regions that hybridize with corresponding regions of a 16S rRNA gene sequence from one or more Mycoplasma species under standard conditions, flanking a central region of non-16S rRNA gene sequence, wherein said 5' and 3' regions hybridize to oligonucleotide primers in said primer set, wherein the step of detecting extension products comprises

gel electrophoresis (see abstract, column 2 last paragraph, columns 3-4 and Examples columns 7-16).

Mckenzie et al does not teach a nucleic acid sequence comprised by a Mycoplasma 16S rRNA gene, wherein the 3'-terminal nucleotide of one or more of said set of primers is selected so as not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein the 3'-terminal two nucleotides of one or more of said set of primers are selected so as not to base pair with an E. coli 16S rRNA gene template if said one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template, further comprising the step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product, wherein the set of oligonucleotide primers comprises a primer selected from the group consisting of: (SEQ ID Nos: 1-4). Mckenzie et al does not explicitly teach the set of oligonucleotide primers detects the presence of Mycoplasma species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium, and M. pirum.*

Webster teaches a nucleic acid sequence (SEQ ID NO: 4) comprised by a Mycoplasma 16S rRNA gene (see SEQ ID NO: 2 in WO 03/006653A1). Although Webster does not explicitly teach one or more of said set of primers is selected whereby one or more of said set of primer does not to base pair with an E. coli 16S rRNA gene template, wherein the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template. Webster does not explicitly teach extending said primers and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein

the 3'-terminal two nucleotides of one or more of said set of primers are selected so as not to base pair with an E. coli 16S rRNA gene template whereby one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template. As provided in the specification that SEQ ID NO: 4 has a 3'-terminal nucleotide is selected (see pg. 28 in the specification) and inherently have the properties of not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein the 3'-terminal two nucleotides of one or more of said set of primers are selected so as not to base pair with an E. coli 16S rRNA gene template if said one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template. As to limitation wherein an oligonucleotide primer that detects the presence of Mycoplasma species M. *pirum* and *Acholeplasma laidlawii*, SEQ ID NO. 4 of Webster et al inherently teach the Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* (see specification pg. 28).

Dodge et al teach an oligonucleotide primer (SEQ ID NO. 2) that detects the presence of Mycoplasma species (see SEQ ID NO. 10 of US Patent No. 6,054278). Although Dodge et al does not explicitly teach a primer that detects the presence of Mycoplasma species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, and M. salivarium.* As provided in the specification (see pg. 27), SEQ ID NO. 2 of Dodge et al is the reverse primer that is conserved with *Mycoplasma* species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium.*

Hartley teaches a step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the

presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product (see columns 4-6).

It would have been prima facie obvious at the time the invention was made to produce a set of oligonucleotide primers taught by Webster and Dodge et al and incorporating uracil DNA glycosylase enzyme according to Hartley because Hartley teach dUTP to permit the destruction of contaminating amplified DNAs and if contamination is detected in a negative control, uracil N-glycosylase can be used since this enzyme cleaves sequences which contain dUTP (see column 4) into a reaction mixture to detect Mycoplasma species taught by McKenzie et al.

Claims 42, 49-51, and 53-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mckenzie et al. 1996 US Patent No. 5,491,062 Feb. 13, 1996 in view of Webster, D WO 03/006653A1 Filing date July 11, 2001, Hartley, J US Patent No. 5,035,996 July 30, 1991 and Dodge et al US Patent No. 6,054278 April 25, 2000.

Claims 42-43, 49-51, and 53-57 are drawn to a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO: 2; extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample.

Mckenzie et al teach a method of detecting the presence of a Mycoplasma species in a sample, the method comprising: drawn to a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample, wherein the step of extending said primers comprises polymerase chain reaction (PCR) amplification, wherein the extension product of a internal control template is detectably different in size or sequence from any extension product resulting

from extension of set primers on a Mycoplasma 16S rRNA gene nucleic acid template, wherein the step, either or before, or concurrent with the step contacting the sample with a set of oligonucleotides, of adding an internal control template to said sample, wherein the step of detecting extension products comprises gel electrophoresis (see abstract, column 2 last paragraph, columns 3-4 and Examples columns 7-16).

Mckenzie et al does not teach a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO: 2; extending at least one of said primers and detecting and extension product, wherein the presence of an extension product indicates the presence of Mycoplasma species in a sample, wherein the step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product, wherein a set of oligonucleotide primers further comprises a primer selected from the group of SEQ ID Nos: 1, 3 and 4. Mckenzie et al does not explicitly teach the set of oligonucleotide primers detects the presence of *Mycoplasma* species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium, and M. pirum.*

Dodge et al teach an oligonucleotide primer (SEQ ID NO. 2) that detects the presence of Mycoplasma species (see SEQ ID NO. 10 of US Patent No. 6,054278). Although Dodge et al does not explicitly teach a primer that detects the presence of Mycoplasma species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, and M. salivarium.* As provided in the specification (see pg. 27), SEQ ID NO. 2 of Dodge et al is the reverse primer that is conserved with Mycoplasma species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium.*

Hartley teaches a step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product (see columns 4-6).

Webster teaches a nucleic acid sequence (SEQ ID NO: 4) comprised by a Mycoplasma 16S rRNA gene (see SEQ ID NO: 2 in WO 03/006653A1). As to limitation wherein an oligonucleotide primer that detects the presence of Mycoplasma species M. *pirum* and *Acholeplasma laidlawii*, SEQ ID NO. 4 of Webster et al inherently teach the Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* (see specification pg. 28).

It would have been prima facie obvious at the time the invention was made to produce a set of oligonucleotide primers taught by Webster and Dodge et al and incorporating uracil DNA glycosylase enzyme according to Hartley because Hartley teach dUTP to permit the destruction of contaminating amplified DNAs and if contamination is detected in a negative control, uracil N-glycosylase can be used since this enzyme cleaves sequences which contain dUTP (see column 4) into a reaction mixture to detect Mycoplasma species taught by McKenzie et al.

Claims 74-75, 77 and 79-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mckenzie et al. 1996 US Patent No. 5,491,062 Feb. 13, 1996 in view of Gunderson et al 1994 Vol. 176 No. 17 pgs. 5244-5254, Webster, D WO 03/006653A1 Filing date July 11, 2001, Hartley, J US Patent No. 5,035,996 July 30, 1991 and Dodge et al US Patent No. 6,054278 April 25, 2000.

Claims 74-75, 77 and 79-89 are drawn to a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO.

3; extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample.

Mckenzie et al teach a method of detecting the presence of a Mycoplasma species in a sample, the method comprising: drawn to a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample, wherein the step, either or before, or concurrent with the step contacting the sample with a set of oligonucleotides, of adding an internal control template to said sample, wherein the step of extension products of internal control template is detectably different in size or sequence from any extension product resulting from extension of a set of primers on a *Mycoplasma* 16S rRNA gene nucleic acid template, wherein the step of extending said primers comprises polymerase chain reaction (PCR) amplification, wherein the step of detecting extension products comprises gel electrophoresis (see abstract, column 2 last paragraph, columns 3-4 and Examples columns 7-16).

Mckenzie et al does not teach a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO: 3; extending at least one of said primers and detecting and extension product, wherein the presence of an extension product indicates the presence of Mycoplasma species in a sample, wherein at east one member of the set of oligonucleotide primers, the 3'-terminal nucleotide is selected such that is does not to base pair with an E. coli 16S rRNA gene template if a member cross-hybridizes with an E. coli 16S rRNA gene template, wherein at least one member of the set of oligonucleotide primers, 3'-terminal two nucleotides are selected such that they do not base pair with an E. coli 16S rRNA gene template if a member cross-hybridizes with said E. coli 16S rRNA gene template, further comprising the step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step

of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product, wherein a set of oligonucleotide primers further comprises a primer selected from the group of SEQ ID Nos: 1, 2, and 3. Mckenzie et al does not explicitly teach the set of oligonucleotide primers detects the presence of *Mycoplasma* species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium, and M. pirum.*

Gunderson et al teaches a nucleic acid sequence (SEQ ID NO: 3) comprised by a *Mycoplasma* 16S rRNA gene (see STIC Report and Results) Although Gunderson et al does not explicitly teach one or more of said set of primers is selected whereby one or more of said set of primer does not to base pair with an E. coli 16S rRNA gene template, wherein the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template. Webster does not explicitly teach extending said primers and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein the 3'-terminal two nucleotides of one or more of said set of primers are selected so as not to base pair with an E. coli 16S rRNA gene template whereby one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template. As provided in the specification that SEQ ID NO: 3 has a 3'-terminal nucleotide is selected (see pg. 28 in the specification) and inherently have the properties of not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein the 3'-terminal two nucleotides of one or more of said set of primers are selected so as not to base pair with an E. coli 16S rRNA gene template if said one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template. As to limitation wherein an oligonucleotide primer that detects the presence of Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* , SEQ ID

NO. 3 of Gunderson et al inherently teach the Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* (see specification pg. 28).

Webster teaches a nucleic acid sequence (SEQ ID NO: 4) comprised by a Mycoplasma 16S rRNA gene (see SEQ ID NO: 2 in WO 03/006653A1). As to limitation wherein an oligonucleotide primer that detects the presence of Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* , SEQ ID NO. 4 of Gunderson et al inherently teach the Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* (see specification pg. 28).

Dodge et al teach an oligonucleotide primer (SEQ ID NO. 2) that detects the presence of Mycoplasma species (see SEQ ID NO. 10 of US Patent No. 6,054278). Although Dodge et al does not explicitly teach a primer that detects the presence of *Mycoplasma* species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, and M. salivarium.* As provided in the specification (see pg. 27) that SEQ ID NO. 2 is the reverse primer that is conserved with *Mycoplasma species* including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium.*

Hartley teaches a step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product (see columns 4-6).

It would have been prima facie obvious at the time the invention was made to produce a set of oligonucleotide primers taught by Gunderson et al, Webster et al and Dodge et al to modify the mixture by incorporating uracil DNA glycosylase enzyme according to Hartley because Hartley teach dUTP to permit the destruction of contaminating amplified DNAs and if contamination is detected in a negative control,

uracil N-glycosylase can be used since this enzyme cleaves sequences which contain dUTP (see column 4) into a reaction mixture to detect Mycoplasma species taught by McKenzie et al.

Claims 90-93, 95, 97-99, and 101-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mckenzie et al. 1996 US Patent No. 5,491,062 Feb. 13, 1996 in view of Webster, D WO 03/006653A1 Filing date July 11, 2001, Hartley, J US Patent No. 5,035,996 July 30, 1991, Gunderson et al 1994 Vol. 176 No. 17 pgs. 5244-5254 and Dodge et al US Patent No. 6,054278 April 25, 2000.

Claims 90-93, 95, 97-99, and 101-105 are drawn to a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample with a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO. 4; extending at least one of said primers and detecting an extension product, wherein the presence of an extension product indicates the presence of a Mycoplasma species in said sample.

Mckenzie et al teach a method of detecting the presence of a Mycoplasma species in a sample, the method comprising: drawn to a method for detecting the presence of a Mycoplasma species in a sample, the method comprising: contacting the sample, wherein the step, either or before, or concurrent with the step contacting the sample with a set of oligonucleotides, of adding an internal control template to said sample, wherein the step of extension products of internal control template is detectably different in size or sequence from any extension product resulting from extension of a set of primers on a *Mycoplasma* 16S rRNA gene nucleic acid template, wherein the step of extending said primers comprises polymerase chain reaction (PCR) amplification, wherein the step of detecting extension products comprises gel electrophoresis (see abstract, column 2 last paragraph, columns 3-4 and Examples columns 7-16).

Mckenzie et al does not teach a set of oligonucleotide primers that hybridize to a 16S rRNA gene sequence in one or more Mycoplasma species, the set of oligonucleotide primers comprising SEQ ID NO: 4; extending at least one of said primers and detecting and extension product, wherein the presence of an extension product indicates the presence of Mycoplasma species in a sample, wherein at east one member of the set of oligonucleotide primers, the 3'-terminal nucleotide is selected such that is does not to base pair with an E. coli 16S rRNA gene template if a member cross-hybridizes with an E. coli 16S rRNA gene template, wherein at least one member of the set of oligonucleotide primers, 3'-terminal two nucleotides are selected such that they do not base pair with an E. coli 16S rRNA gene template if a member cross-hybridizes with said E. coli 16S rRNA gene template, further comprising the step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product, wherein a set of oligonucleotide primers further comprises a primer selected from the group of SEQ ID Nos: 1, 2, and 3. Mckenzie et al does not explicitly teach the set of oligonucleotide primers detects the presence of *Mycoplasma* species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium, and M. pirum.*

Webster teaches a nucleic acid sequence (SEQ ID NO: 4) comprised by a *Mycoplasma* 16S rRNA gene (see SEQ ID NO: 2 in WO 03/006653A1). Although Webster does not explicitly teach one or more of said set of primers is selected whereby one or more of said set of primer does not to base pair with an E. coli 16S rRNA gene template, wherein the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template. Webster does not explicitly teach extending said primers and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein the 3'-terminal two nucleotides of one or more of said set of primers are selected so as

not to base pair with an E. coli 16S rRNA gene template whereby one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template. As provided in the specification that SEQ ID NO: 4 has a 3'-terminal nucleotide is selected (see pg. 28 in the specification) and inherently have the properties of not to base pair with an E. coli 16S rRNA gene template if the oligonucleotide primer cross-hybridizes with said E. coli 16S rRNA gene template, extending said primers, and detecting extension products of said primers, wherein the presence of an extension product is indicative of the presence of a Mycoplasma species in said sample, wherein the 3'-terminal two nucleotides of one or more of said set of primers are selected so as not to base pair with an E. coli 16S rRNA gene template if said one or more of said set of oligonucleotide primers cross-hybridizes with said E. coli 16S rRNA gene template. As to limitation wherein an oligonucleotide primer that detects the presence of Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* , SEQ ID NO. 4 of Webster inherently teach the Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* (see specification pg. 28).

Gunderson et al teaches a nucleic acid sequence (SEQ ID NO: 3) comprised by a Mycoplasma 16S rRNA gene (see STIC Report Results). As to limitation wherein an oligonucleotide primer that detects the presence of Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* , SEQ ID NO. 3 of Gunderson et al inherently teach the Mycoplasma species M. *pirum* and *Acholeplasma laidlawii* (see specification pg. 28).

Dodge et al teach an oligonucleotide primer (SEQ ID NO. 2) that detects the presence of Mycoplasma species (see SEQ ID NO. 10 of US Patent No. 6,054278). Although Dodge et al does not explicitly teach a primer that detects the presence of *Mycoplasma* species including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, and M. salivarium.* As provided in the specification (see pg. 27) that SEQ ID NO. 2 is the reverse primer that is conserved with *Mycoplasma species* including *Acholeplasma laidlawii, Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. salivarium.*

Hartley teaches a step, before the step of extending said primers, of contacting said reaction mixture with a uracil DNA glycosylase enzyme, wherein said reaction mixture comprises dUTP, wherein the step of extending said primers is performed in the presence of dUTP, and wherein said extending results in the incorporation of dUTP into an extension product (see columns 4-6).

It would have been prima facie obvious at the time the invention was made to produce a set of oligonucleotide primers taught by Webster, Gunderson et al and Dodge et al to modify the mixture by incorporating uracil DNA glycosylase enzyme according to Hartley because Hartley teach dUTP to permit the destruction of contaminating amplified DNAs and if contamination is detected in a negative control, uracil N-glycosylase can be used since this enzyme cleaves sequences which contain dUTP (see column 4) into a reaction mixture to detect Mycoplasma species taught by McKenzie et al.

Status of the Claims

7. No claims are allowed.

Claims 1-27 are withdrawn.

Claims 38-40, 44-46, 58-73, 76, 78, 94 and 96 are objected to as being dependent upon a rejected base claim.

Claims 28-105 are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner
GAU 1645
REM 3B31

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PRIMARY EXAMINER